oral pesticide,

d. is substantially resistant to proteolysis by trypsin and proteinase K, and

e. has its pesticidal activity substantially destroyed by treatment with sodium dodecyl sulphate or acetone on heating to 80°C.

50. (Amended) A method for killing or controlling insect pests, which method comprises administering orally to the insect a composition according to claim 41.

A marked-up version of the amended claims is attached.

REMARKS

The November 20, 2001 Official Action and the single reference cited therein have been carefully considered. In view of the amendments presented herewith and the following remarks, favorable reconsideration and allowance of this application are respectfully requested.

At the outset, it is noted that a shortened statutory response period of three (3) months was set forth in the November 20, 2001 Official Action. The initial due date for response, therefore, was February 20, 2002. A petition for a three (3) month extension of the response period is submitted with this response, which is being filed within the three (3) month

extension period.

In the November 20, 2001 Official Action, claims 37-49 have been rejected for allegedly failing to comply with the written description requirement of 35 U.S.C. §112, first paragraph. In this connection, the Examiner maintains the position that because the present specification does not provide sequence information for the protein recited in claim 37, an adequate written description of the claimed invention is allegedly lacking.

Claims 37-49 have been further rejected under 35 U.S.C. §112, first paragraph as allegedly failing to provide a sufficiently enabling disclosure. This ground of rejection has been maintained from the preceding Official Action. In connection with this ground of rejection, the Examiner asserts that the present specification does not teach how to make or use an specific pesticidal proteins, as called for in applicants' claims.

Also in the November 20, 2001 Official Action, the prior art rejection under 35 U.S.C. §102(e) based on U.S. Patent No. 5,516,318 to Dudney has been maintained with respect to claims 41 and 46-48.

Claim 50 has also been rejected as allegedly indefinite under 35 U.S.C. §112, second paragraph, as it is dependent from a canceled claim.

Claim 40 stands further rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking a written description for

the recitation "550C". The Examiner correctly noted that this recitation is a typographical error which would be remedied by amending the claim to read "55°C".

The foregoing rejections constitute all of the grounds set forth in the November 20, 2001 Official Action for refusing the present application.

In accordance with the present amendments, claim 37 has been amended to further characterize the "variant" recited therein as one which is obtained from *Xenorhabdus nematophilus*, the sequence of which hybridizes with the sequence of Figure 2 under stringent conditions. In addition, claim 40 has been amended, as suggested by the Examiner, to overcome the 35 U.S.C. §112, first paragraph rejection thereof based on the above-noted typographical error.

Claim 50 has been amended to make it dependent on claim 41, rather than claim 5, which had been canceled.

No new matter has been introduced into this application by reason of any of the amendments presented herewith.

As a result of the present amendments, the rejection of claim 40 under 35 U.S.C. §112, first paragraph, due to the above-noted typographical error has been overcome, as has the §112, second paragraph rejection of claim 50. Thus, the only grounds of rejection that remain to be addressed are the lack of written description rejection of claims 37-49, the inadequate enablement rejection of claims 37-49 and the prior art rejection of claims 41 and 46-48 based on Dudney. These last mentioned

three (3) grounds of rejection are respectfully traversed.

Turning first to the rejection alleging lack of written description for the protein claimed in claims 37-49, applicants respectfully submit that the Examiner has failed to carry the PTO's burden of proof by establishing a person skilled in the art would not recognize in applicants' specification disclosure a description of the invention defined by the present claims. The Examiner's sole criticism of applicants' claims in this regard is that no protein sequence information is provided in the present specification. There is no dispute that this is the case. However, neither the case law nor current PTO guidelines or practice require sequence information under the facts of this case.

The case law cited in support of the Examiner's position is readily distinguishable from the present case. Applicants are not attempting to claim a nucleic acid sequence based on isolation of a protein, in combination with a probing strategy for recovering the claimed gene, as was the situation in Fiers v. Revel. Nor are applicants attempting to claim a broad class of growth factors based on disclosure of growth factor from a single species plus a DNA sequence that theoretically encodes such factors, as was attempted in Fiddes v. Baird. Nor are applicants attempting to claim a c-DNA without providing relevant structural or physical characteristics as was done in University of California v. Eli Lilly & Co.

In the present case, by contrast to those cited by the Examiner, applicants have provided a reference sequence encoding demonstrated oral activity (SEQ. ID. No. 1 from clone 1 of NCIMB40877). Furthermore, applicants disclose that the toxicity may be transferred to E. coli through SEQ. ID No. 1 and retain the unexpected oral toxicity (see Examples 7-9).

As for the location of the coding sequences that are present within SEQ. ID. No. 1, of course this is something which can be analyzed computationally, as noted in applicants' previous response. In terms of activity of the ORFs thus identified, the Examiner's attention is respectfully directed to the present specification at page 8, first two paragraphs, which disclose that portions of SEQ. ID. No. 1 encoding pesticidal agents may, if desired, be identified by use of conventional techniques available to those skilled in the art. One particular method (transposon mutagenesis, as taught by Siefert et al. (1986)) is cited. The specification discloses that the sequence from the cosmid clone (SEQ. ID. No. 1) may be electroporated into E. coli and a transposon mTn3(HIS3) used in insertion mutagenesis. DNA sequencing can then be used to identify regions showing particular activity. Applicants' subsequently published paper, Applied And Environmental Microbiology, 67 (5):2062-69 (May 2001) (copy enclosed) provides evidence that the particular active genes encoded by the cosmid disclosed in the present application (corresponding to SEQ. ID. No. 1 - c*HRIM1*) are readily identified in precisely the manner explicitly taught by reference to Siefert

et al. in the present application (insertion mutagenesis using transposon mTn3(HIS3) - see page 2063, column 1, final paragraph). Applicants' publication thus confirms the teaching of the present specification, as well as the importance of the genes of SEQ. ID. No. 1 as a "pathogenicity island" in the *Xenorhabdus nematophilus*.

Claim 40 also provides an enumeration of characteristics that serve to prove that applicants were in possession of the claimed invention at the time the present application was filed.

It is further noted in this regard that the PTO has granted a number of recent patents having claims directed to proteins, in which no SEQ. ID. No. is recited. These include, for example, U.S. Patent Nos. 5,863,895, 5,981,255, 5,986,050, 6,379,719, 6,383,550 and 6,383,551. In that the statutory requirements for patentability must be uniformly applied to all applicants, the claims of the present application should be accepted as satisfying the written description requirement of §112 for the same reasons that the claims of the aforementioned patents were found to have satisfied this requirement.

Regarding enablement, the specification discloses both methods of producing and using the claimed toxins directly from *Xenorhabdus*. See, e.g. Examples 1-6.

It should also be noted that claim 37, as now amended, is drawn to the protein encoded by the nucleic acid sequence of SEQ. ID. No. 1 or by a variant obtained from *Xenorhabdus*

nematophilus, the sequence of such variant hybridizing with the sequence of SEQ. ID. No. 1 under stringent conditions. The enablement provided in the present specification is clearly commensurate in scope with these amended claims. As previously noted, the present application discloses a nucleotide sequence from *Xenorhabdus nematophilus* (NCIMB 40887) which is useful, in whole or in part as an important insecticidal toxin. The data provided in the present specification further demonstrate that other *Xenorhabdus nematophilus* sources contain closely related sequences which were identified using hybridization (note the 11.4 KB and 9 KB fragments of NCIMB 40886 and ATCC 19061, discussed in Example 11) and that these organisms encode the same unexpected oral activity of SEQ. ID. No. 1 (see Examples 6-9).

The unduly rigid interpretation of the enablement requirement of §112 which the Examiner seeks to impose in this case, effectively disregards the adverse consequences of having applicants confine their claims to the nucleotide sequence of SEQ. ID. No. 1. The resultant claims could easily be circumvented by the simple expedient of identifying useful insecticidally active variants by means of routine procedures of the type disclosed by applicants herein. The availability of such an option would be self-evident to those skilled in the art upon consideration of applicants' disclosure. It cannot reasonably be maintained that such a blatantly inequitable result is permissible under the U.S. patent laws. Support for applicants' position in this regard is found in In re Goffe, 191

U.S.P.Q. 429 (C.C.P.A. 1976), wherein the Court stated at 431:

> For all practical purposes, the Board would limit appellant to claims involving specific materials disclosed in the examples, so that a competitor seeking to avoid infringing the claims would merely have to follow the disclosure in the subsequently issued patent to find a substitute. However, to provide effective incentives, claims must adequately protect inventors. To demand that the first to disclose shall limit his claim to what he has found will work or to materials which meet the guidelines specified for 'preferred' materials in the process such as the one herein involved would not serve the constitutional purpose of promoting progress in the useful arts. [citation omitted.]

In the present case, just as in Goffe, applicants are entitled to protection commensurate with their disclosure, and such variants should therefore properly be included in applicants' claims, along with SEQ. ID. No. 1.

As for the prior art rejection based on Dudney, which the Examiner has maintained with respect to claims 41 and 46-48, the Examiner contends that the insecticidally active agent of applicants' claims would be inherently produced by the *Xenorhabdus nematophilus* strains disclosed by Dudney. The disclosure of Dudney, however, directly contradicts the Examiner's position in this regard.

The law is well settled that inherency, when asserted by the PTO, must be a necessary result and not merely a possible result. Ex parte Keith 154 U.S.P.Q. 320 (Bd. of Pat. Apps. 1966). Dudney describes two strains of *Xenorhabdus nematophilus*, identified as strain 19061/1 and strain Im/1, which were tested for fire ant control. After treatment of fire ant mounds with

these agents, fire ant activity was still observed in mounds treated with strain 19061/1, whereas no ant activity at all was observed in mounds treated with strain Im/1. Thus, these two (2) agents were not equally effective. Moreover, when field trials were carried out, the only strain tested was Im/1 (deposited October 25, 1996 which is after applicants' effective filing date), thus raising a question as to the practical utility of stain 19061/1. These test results reported by Dudney clearly demonstrate that all strains of *Xenorhabdus nematophilus* either produce different proteins, or the same proteins in different amounts which affect the biological activity thereof. It necessarily follows, therefore, that all strains of *Xenorhabdus nematophilus* do not inherently produce the same insecticidal activity.

In view of the present amendments and the foregoing remarks, it is respectfully requested that the grounds of rejection set forth in the November 20, 2001 Official Action be withdrawn and that this application be passed to issue, and such action is earnestly solicited.

Respectfully submitted,

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Marked-Up Version of Amended Claims

37. (Amended) An isolated pesticidal agent which is an extracellular protein obtainable from a *Xenorhabdus nematophilus* species and which is encoded by the nucleotide sequence of Figure 2 (SEQ ID No 1) or encoded by a variant [thereof which hybridizes] obtained from *Xenorhabdus nematophilus*, the sequence of said variant hybridizing with said sequence of Figure 2 under stringent conditions, said protein having toxic activity when administered orally to an insect.

40. (Amended) An agent according to claim 37, which

a. has oral pesticidal activity against *Pieris brassicae*, *Pieris rapae* and *Plutella xylostella*,

b. is substantially heat stable to [550C] 55°C,

c. acts synergistically with *B. thuringiensis* cells as an oral pesticide,

d. is substantially resistant to proteolysis by trypsin and proteinase K, and

e. has its pesticidal activity substantially destroyed by treatment with sodium dodecyl sulphate or acetone on heating to 80°C.

50. (Amended) A method for killing or controlling insect pests, which method comprises administering orally to the insect a composition according to claim [5] 41.